

Animal Study Protocol Review – Regulatory Source Language

U.S. Government Principles

PHS Policy

Animal Welfare Regulations (AWR - USDA)

Guide for the Care and Use of Laboratory Animals (*Guide*)

ASP Form (online form) & PQFs

I, II - Personnel, Qualifications and Training

- Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living animals. Adequate arrangements shall be made for their in-service training, including the proper and humane care and use of laboratory animals.
- Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures.
(also AWR)
- The following topics should be considered...: adequacy of training and experience of personnel in the procedures used, and roles and responsibilities of the personnel involved

IV - Description of the Work Proposed; Scientific Justification

- Procedures involving animals should be designed and performed with due consideration of their scientific relevance to human or animal health, the advancement of knowledge, or the good of society.
- Applications and proposals... that involve the care and use of animals shall contain the following: ...c) a complete description of the proposed use of the animals...
- A proposal...must contain the following: ... (3) A complete description of the proposed use of the animals...
- The following topics should be considered...: rationale and purpose of the proposed use of animals; a clear and concise sequential description of the procedures involving the use of animals that is easily understood by all members of the committee

V, VI - Consideration of alternatives to pain/distress (category D or E)

- The principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources, e.g., the Animal Welfare Information Center, used to determine that alternatives were not available.
- The following topics should be considered...: availability or appropriateness of the use of less invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation

VI - Animal Information

- The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results.
- Applications and proposals...that involve the care and use of animals shall contain the following: a.) Identification of the species and the approximate number of animals to be used; b.) rationale for involving animals, and for the appropriateness of the species and numbers of animals to be used.
- A proposal...must contain the following: (1) Identification of the species and approximate number of animals to be used; (2) A rationale for involving animals, and for the appropriateness of the species and numbers of animals to be used...

VII - Animal Housing

- The living conditions of animals should be appropriate for their species and contribute to their health and comfort.
(also PHS Policy and AWR)
- the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied.
(also PHS Policy)
- Medical care for animals will be available and provided as necessary by a qualified veterinarian.
- The housing, feeding, and nonmedical care of the animals will be directed by the attending veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied.... Medical care for animals will be available and provided as necessary by a qualified veterinarian.

VII - Exceptions

- Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group such as an institutional animal care and use committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.
- The following topics should be considered...: nonstandard housing and husbandry requirements (See Section M below for other exceptions/exemptions)

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Section E: Experimental Design

PI has provided a description of the work that includes the overall goals/value of the research

- Procedures involving animals should be designed and performed with due consideration of their scientific relevance to human or animal health, the advancement of knowledge, or the good of society.
- The PI has provided written Assurance that the activities do not unnecessarily duplicate previous experiments.
- The following topics should be considered...: availability or appropriateness of the use of less invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation

Content of the protocol/application must include:

- A complete description of the proposed use of the animals (also AWR)
- The PI has provided written Assurance that the activities do not unnecessarily duplicate previous experiments.
- The following topics should be considered...: rationale and purpose of the proposed use of animals; a clear and concise sequential description of the procedures involving the use of animals that is easily understood by all members of the committee; unnecessary duplication of experiments

Appropriateness of species and animal numbers:

- The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results.
- Identification of the species and the approximate number of animals to be used; b.) rationale for involving animals, and for the appropriateness of the species and numbers of animals to be used... (also AWR)
- The following topics should be considered...: justification of the species and number of animals proposed; whenever possible, the number of animals and experimental group sizes should be statistically justified

Humane Endpoints:

- Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure or, if appropriate, during the procedure.
- Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly killed at the end of the procedure or, if appropriate, during the procedure. (also AWR)
- The following topics should be considered...: description and rationale for anticipated or selected endpoints; criteria and process for timely intervention, removal of animals from a study, or euthanasia if painful or stressful outcomes are anticipated

Euthanasia:

- Methods of euthanasia will be consistent with the recommendations of the AVMA Panel on Euthanasia, unless a deviation is justified for scientific reasons in writing by the investigator [and approved by the IACUC].
- Methods of euthanasia used must be in accordance with the definition of the term set forth in 9 CFR part 1, §1.1 of this subchapter, unless a deviation is justified for scientific reasons, in writing, by the investigator.
- The following topics should be considered...: method of euthanasia or disposition of animals, including planning for care of long-lived species after study completion

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Section G: Anesthetic Procedures

General:

- Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.
- Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia unless the procedure is justified for scientific reasons in writing by the investigator (and approved by the IACUC).
(also USGP and AWR)
- A description of procedures designed to assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research, including provision for the use of analgesic, anesthetic, and tranquilizing drugs where indicated and appropriate to minimize discomfort and pain to animals.
- The following topics should be considered...: impact of the proposed procedures on the animals' well-being

Minimization of Discomfort/Use of anesthesia:

- Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.
- Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design
- Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator (and approved by the IACUC).
- Procedures that may cause more than momentary or slight pain or distress to the animals will: (A) Be performed with appropriate sedatives, analgesics or anesthetics, unless withholding such agents is justified for scientific reasons, in writing, by the principal investigator and will continue for only the necessary period of time; (B) Involve, in their planning, consultation with the attending veterinarian or his or her designee; (C) Not include the use of paralytics without anesthesia.
- Successful surgical outcomes require appropriate attention to presurgical planning, personnel training, anesthesia, aseptic and surgical technique, assessment of animal well-being, appropriate use of analgesics, and animal physiologic status during all phases of a protocol involving surgery and postoperative care.

Multiple Surgical procedures:

- No animal will be used in more than one major operative procedure from which it is allowed to recover, unless: (A) justified for scientific reasons by the principal investigator, in writing; (B) Required as routine veterinary procedure or to protect the health or well-being of the animal as determined by the attending veterinarian, or (C) In other special circumstances as determined by the Administrator on an individual basis.
- The following topics should be considered...: appropriate sedation, analgesia, and anesthesia (indices of pain or invasiveness might aid in the preparation and review of protocols; conduct of surgical procedures, including multiple operative procedures; postprocedural care and observation (e.g., inclusion of post-treatment or postsurgical animal assessment forms)

Pre- Intra- Post- procedures and care

- Activities that involve surgery include appropriate provision for pre-operative and post-operative care of the animals in accordance with established veterinary medical and nursing practices. All survival surgery will be performed using aseptic procedures, including surgical gloves, masks, sterile instruments, and aseptic techniques.
- Preemptive analgesia (the administration of preoperative and intraoperative analgesia) enhances intraoperative patient stability and optimizes postoperative care and well-being by reducing postoperative pain (Coderre et al. 1993; Hedenqvist et al. 2000).
- [Intraoperative] Monitoring includes routine evaluation of anesthetic depth and physiologic functions and conditions, such as body temperature, cardiac and respiratory rates and pattern (Flegal et al. 2009), and blood pressure (Kuhlman 2008), and should be appropriately documented... Fluid replacement may be a necessary component of intraoperative therapy depending on the duration and nature of the procedure. For aquatic species (including amphibians), care should be taken to keep the skin surfaces moist and minimize drying during surgical procedures.
- During this [postoperative] period, animals should be in a clean, dry, and comfortable area where they can be observed frequently by trained personnel. Particular attention should be given to thermoregulation, cardiovascular and respiratory function, electrolyte and fluid balance, and management of postoperative pain or discomfort. Additional care may be warranted, including long-term administration of parenteral fluids, analgesics, and other drugs, as well as care of surgical incisions. Appropriate medical records should also be maintained.

Surgical Facilities

- Major operative procedures on non-rodents will be conducted only in facilities intended for that purpose which shall be operated and maintained under aseptic conditions.
- Non-major operative procedures and all surgery on rodents do not require a dedicated facility, but must be performed using aseptic procedures.
- Operative procedures conducted at field sites need not be performed in dedicated facilities, but must be performed using aseptic procedures;

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Section F: Hazardous agents

- The following topics should be considered...: use of hazardous materials and provision of a safe working environment.
- Institutions should have written policies and procedures governing experimentation with hazardous biologic, chemical, and physical agents. An oversight process (such as the use of a safety committee) should be developed to involve persons who are knowledgeable in the evaluation and safe use of hazardous materials or procedures and should include review of the procedures and facilities to be used for specific safety concerns. Formal safety programs should be established to assess hazards, determine the safeguards needed for their control, and ensure that staff have the necessary training and skills and that facilities are adequate for the safe conduct of the research.

Section M: Exceptions

- Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group such as an institutional animal care and use committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.
- The following topics should be considered...: nonstandard housing and husbandry requirements
- Enrichment programs should be reviewed by the IACUC, researchers, and veterinarian on a regular basis to ensure that they are beneficial to animal well-being and consistent with the goals of animal use. They should be updated as needed to ensure that they reflect current knowledge. Personnel responsible for animal care and husbandry should receive training in the behavioral biology of the species they work with to appropriately monitor the effects of enrichment as well as identify the development of adverse or abnormal behaviors.
- Regulation of food or fluid intake may be required for the conduct of some physiological, neuroscience, and behavioral research protocols. The objective when these studies are being planned and executed should be to use the least restriction necessary to achieve the scientific objective while maintaining animal well-being.
- Prolonged restraint, ...should be avoided unless it is essential for achieving research objectives and is specifically approved by the IACUC
- The use of pharmaceutical-grade chemicals and other substances ensures that toxic or unwanted side effects are not introduced into studies conducted with experimental animals. They should therefore be used, when available, for all animal-related procedures (USDA 1997b). The use of non-pharmaceutical-grade chemicals or substances should be described and justified in the animal use protocol and be approved by the IACUC